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Abstract: Background and Study Object A leak-proof dura closure after elective surgery for intradural spinal lesions is important to achieve an uncomplicated postoperative course. Because many different closure techniques and dura substitutes exist, we tried to identify the superior material and technique to avoid cerebrospinal fluid leaks (CSFLs).Patients and Methods Between 2004 and 2009, 91 patients underwent surgical treatment of intradural spinal pathologies with primary dura closure with or without the use of dura substitutes at our institution. Pre- and postoperative images and the clinical course were analyzed retrospectively with respect to the occurrence of CSFL.Results In 34% of the 91 patients, radiological signs of CSFL were observed. A total of 12 patients (13%) were symptomatic for CSFL and required a single puncture, lumbar drain, or surgical revision. No significant relation between CSFL and patient characteristics, underlying diagnosis, localization, or extension was noted. In contrast, the incidence of CSFL was significantly increased if more than one substitute for dura closure was used. The results showed that 41.7% of these patients showed radiological signs of CSFL as compared with 10.4% of patients in which only a single material was used.Conclusion In our study, none of the applied products appeared to be superior to the others. Surgery with the combined use of multiple dura closure substitutes was associated with the enhanced incidence of postoperative CSFL. However, our findings concerning the various dura sealants could not be used to compare those different materials, due to the great variety of combinations of dura sealants and the retrospective analysis of the data.

DOI: https://doi.org/10.1055/s-0032-1304809

Cerebrospinal Fluid Leaks after Planned Intradural Spine Surgery: a Single-Center Analysis of 91 Cases

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Abstract

Background and Study Object: A leak-proof dura closure after elective surgery for intradural spinal lesions is important to achieve an uncomplicated postoperative course. Because many different closure techniques and dura substitutes exist, we analyzed the superior closure to avoid cerebrospinal fluid leaks (CSFL).

Patients and Methods: Between 2004 and 2009, 91 patients underwent surgical treatment of intradural spinal pathologies with primary dura closure with or without the use of dura substitutes at our institution. Pre- and postoperative images and the clinical course were analyzed retrospectively with respect to the occurrence of CSFL.

Results: In 34% of the 91 patients, radiological signs of CSFL were observed. Twelve patients (13%) were symptomatic for CSFL and required a single puncture, lumbar drain or surgical revision. No significant effect of CSFL regarding patient characteristics, underlying diagnosis, localization or extension grade was noted. In contrast, the incidence of CSFL was significantly increased if more than one substitute for dura closure was used. The results showed that 41.7% of these patients showed radiological signs of CSFL as compared to 10.4% of patients in whom only a single material was used.

Conclusion: In our study, none of the applied products appeared to be superior to the others. Surgery with the combined use of multiple dura closure substitutes was associated with the enhanced incidence of postoperative CSFL. However, our findings concerning the various dura sealants could not be used to compare those different materials, due to the great variety of combinations of dura sealants and the retrospective analysis of the data.

Keywords

Cerebrospinal fluid leaks (CSFL), intradural spinal lesion, leak-proof dura closure, neurosurgery, resection

Zusammenfassung

Zielsetzung: Um einen unkomplizierten postoperativen klinischen Verlauf nach intraduralen spinalen Operationen zu garantieren ist der lecksichere Duraverschluss entscheidend. Aus diesem Grund analysieren wir in dieser Studie den besseren Duraverschluss zur Verhinderung eines Liquorlecks.

Patienten und Methoden: In unsere Abteilung wurden zwischen 2004 und 2009 91 Patienten mit intraduralen spinalen Läsionen operiert und der primäre Duraverschluss erfolgte sowohl mit als auch ohne Hilfe eines Duraersatzmaterials. Die prä- und postoperative Bildgebung und der klinischer Verlauf dieser Patienten wurde retrospektive bezüglich dem Auftreten eines Liquorlecks analysiert.

Resultate: 34% der 91 Patienten zeigten radiologische Anzeichen eines Liquorlecks. Zwölf dieser Patienten (13%) waren zudem klinisch symptomatisch und benötigten eine Lumalpunktion, Lumbaldrainage oder chirurgische Intervention. Patienteneigenschaften, -diagnose, Lokalisation der spinalen Läsion und Resektionsgrad zeigten keine statistische Signifikanz bezüglich des Auftretens eines Duralecks. Dagegen zeigte sich, dass die Anzahl der verwendeten Materialien für den Duraersatz signifikant mit dem Auftreten eines Duralecks korrelierte. 41.7% dieser Patienten zeigte radiologische Zeichen eines Liquorlecks im Gegensatz zu 10.4% der Patienten, die nur mit einem Duraersatzmaterial operiert wurden.

Schlussfolgerung: In dieser Studie zeigten wir, dass keines der verwendeten Materialien zum Duraverschluss den anderen überlegen scheint und dass die Kombination von mehreren Materialien mit einem höheren Auftreten eines postoperativen Duralecks einhergehen kann.

Introduction

Cerebrospinal fluid leak (CSFL) is among the most prevalent postoperative complications after intradural spinal surgery and affects approximately 5-13% of surgically treated patients.[9,11,17,18,20,25] Although most of the CSFLs are asymptomatic, they can cause further complications such as postoperative meningitis, arachnoiditis or epidural abscess as well as spino-cutaneous fistulas, pseudomeningocele or CSFL syndrome associated with chronic pain, radiculopathy and postural headaches.[3,12] Aside from symptomatic treatment, interventions such as single puncture or lumbar drain are typically sufficient during the postoperative course to treat CSFL; a surgical revision is rarely needed.[4] Numerous surgical techniques and technical aids have been described for use in dura closure after incidental durotomy, but the best method to achieve a watertight dural repair remains controversial.[5,10,13,16,21-24,26,28,29,32] To the best of our knowledge, systematic evaluation of the incidence of CSFL after planned durotomy in spinal intradural surgery has not been analyzed. Therefore, the aim of our study was to evaluate the incidence of CSFLs after planned durotomy based on radiological and clinical features with a focus on initial closure of the dura.

Materials and Methods

General patient characteristics

We performed a retrospective analysis of all 112 consecutive spinal intradural pathologies between 2004 and 2009 at the Department of Neurosurgery that were surgically treated with planned durotomy. We excluded 21 cases of revision surgery. The final series consisted of 91 first-time surgical procedures in 46 male (50.5%) and 45 female (49.5%) patients. The location of the pathologies was extramedullary in 51 cases (56%) and

intramedullary in 40 cases (44%). The lesion was located in the cervical spine in 30 cases (33%), in the thoracic spine in 28 cases (31%) and in the lumbar spine in 33 cases (36%).

Surgery and dura closure

Operations were performed through a posterior midline approach using microsurgical techniques by multiple senior neurosurgeons in our department. In all cases, direct primary running sutures were placed as previously described; in some cases, additional single stitches were used.[1,2] Additionally, any one of six dura closure substitutes and/or two hemostatic products (Tab. 1) were used depending on the surgeon's assessment of necessity. No autologous dura substitute, such as the fascia lumbodorsalis, was used. Postoperative management of all patients with spinal dural repair consisted of having the patient lie flat for 24 hours.

Study design

Our primary endpoint of interest was the occurrence of CSFL based on postoperative clinical and radiological examinations. Basic demographic data (age and sex), length of hospital stay, method of dura closure, need for further intervention (single puncture, lumbar drain or surgical revision) and surgical extent (single or multi-level) as related to the occurrence of CSFL were investigated (Table 2). Spinal lesions were grouped based on their intra- or extramedullary localization as well as on histopathological features (Table 3). Based on the operative record, the modality of dura opening was categorized as being standard (straight durotomies in the posterior midline, no involvement of the dura in the pathologic process) or complex (e.g. atypically shaped incisions, involvement of the dura in the pathologic process, incision not in the midline, incision towards the roots, excision of the dura).

Among the group of patients presenting with CSFL, the following two subgroups were defined: (i) CSFL was present, but did not require further treatment and (ii) CSFL was symptomatic and needed to be treated. CSFL was categorized as being symptomatic when a marked palpable swelling was recognized, CSF secretion was present through the wound or clinical signs of neuro-compression occurred.

Statistical analysis and neuroimaging

Statistical data analysis was performed using Microsoft Excel and SPSS. The association between the investigated parameters was analyzed by t-tests, one-way ANOVA and cross-tabulation with Fisher's exact test. P-values < 0.05 were considered to be statistically significant.

Postoperative imaging (MRI) was performed within 72 hours after surgery and evaluated regarding CSFL by an independent senior board-certified neuroradiologist. CSFL was radiographically defined as the presence of T2 hyperintense fluid collections surrounding the spinal canal at the site of the intervention in the post- as compared to the preoperative MRI.

Results

Among the 91 patients, 32 (34%) showed radiological signs of CSF effusion on the postoperative MRI. Twelve patients (13%) required further interventions to treat the CSFL: in two patients, a single puncture was sufficient to treat the CSFL; in four patients, a lumbar drain was needed; and in six patients, surgical revision was needed. Between these 12 patients and the other 20 patients who did not require further treatment, no significant difference in age (Tab. 2, p=0.3), sex (Tab. 2, p=0.4), length of hospital stay (Tab. 2, p=0.4) or extent of the surgical approach (Tab. 2, p=0.7) was noted. The mean extent of spinal involvement in the

investigated patients was 2.2 segments. Additionally, with regard to localization of the lesion, there were no statistically significant differences in the intra- or extramedullary localization of the lesion (Tab. 2, p=0.3). No statistically significant correlation among any of the three most common tumor entities in our series (extramedullary meningioma; extramedullary neurinomas and neuroepithelial tumors) and the incidence of CSFL was found (Tab. 3, p=0.2).

When evaluating the various products to enhance dura closure and hemostatic materials, no single product was superior in avoiding the incidence of CSFL (Tab. 4). However, when analyzing the incidence of CSF leaks with regard to the amount of product applied for dura closure, we found a significantly higher rate of CSFL in patients where more than one product had been used during the procedure as compared to the use of a single product only (Fig. 1, p=0.03). The combination of more than one dura substitute or hemostatic material was associated with a significantly higher incidence of both spontaneously resolving CSFL and CSFL that ultimately required further treatment. Even when the two hemostatic products were excluded from the analysis, the results remained consistently significant (p=0.028).

The modality by which the durotomy was performed did not show any statistically significant relationship with the formation of CSFL (Tab. 2, p=0.7).

Discussion

Incidence of CSF leaks

Achieving a leak-proof dura closure after intradural spinal surgery is important to prevent CSFL and the associated complications. In this context, the primary suture is the method of choice for dura closure after planned spinal durotomy.[2,6,8,12] In a series of 115 patients, Jenkinson et al. described a 10% risk of CSFL with their technique of primary suture without the use of dura substitutes.[17] These results are similar to those in our series, which revealed a 10.4% risk of CSFL in primary suturing with the use of dura closure substitutes

alone. One could argue that dura substitutes are not promising at all because our overall CSFL risk was similar to that reported in Jenkinson´s study, which did not use any dura substitute. However, our findings concerning the various dura sealants could not be used to compare those different materials, due to the great variety of combinations of dura sealants and the retrospective analysis of the data. To this end, a prospective randomized study is necessary. In a review regarding surgery on intraspinal cord tumors, which included 360 patients, Brotchi et al. described an overall surgical complication rate of 4% including cerebrospinal fluid fistulas and meningocele.[7] However, the authors did not mention whether CSFL was diagnosed based on clinical or radiological findings. In our study, we diagnosed CSFL based on both clinical and radiological findings. This approach is highly sensitive and allows for early detection of CSFLs and the timely initiation of the appropriate therapy.

Effect of dura substitutes on the occurrence of CSF leaks

To the best of our knowledge, this is the first report on dura repair that has investigated the application of several dura substitutes. However, there were different sources of variability present in our study. (i) Patient characteristics, lesion location and lesion pathology varied. (ii) The surgeons differed in their assessments and preferences with respect to surgical approaches or materials. (iii) The number of dura substitutes was larger than the number of patients in the study.

As a first result, we showed that none of these substitutes were superior compared to the others in single use. Our failure to observe a significant difference for any of the products may be due to the large number of products tested. However, it may reflect the preference of the surgeon for different products in different surgical situations. As a second result, we found that the combined use of different substitutes is associated with the enhanced occurrence of CSFL (cross-tabulation $p = 0.03$). The reason for this may be that interactions between the various dura closure substitutes and hemostatic products might compromise physiological

scarring and wound healing. Another possibility may apply during surgery and before dura closure. We hypothesize that when the surgeon anticipates difficulties in achieving leak-proof dura closure, he or she uses a higher amount and several types of artificial material. Thus, surgical interventions presenting themselves as more complicated to the surgeon lead to both an enhanced use of dura closure aids as well as an increased incidence of CSF leaks. Therefore, the use of multiple dura products or substitutes could represent a difficult intra-operative situation or a lack of experience on the part of the surgeon, resulting in a higher incidence of CSFL.

Dura substitutes and hemostatic products in the literature

In previous studies, many dura closure substitutes, which consist of auto-, allograft or synthetic material, and hemostatic products were used to enhance the closure of the dura after durotomies.[3,4,13,15,23,26,29] Most of these studies investigated the use of dura closure substitutes in incidental rather than planned durotomies. For instance, Jankowitz et al. published a retrospective analysis of 4835 spinal surgical procedures and demonstrated that the use of fibrin glue did not significantly decrease the incidence of CSFL after incidental durotomy.[16] Therefore, the authors did not recommend the use of fibrin glue in addition to primary suture of the dura. The only univariate predictor for CSFL in that study was prior spinal surgery, which increased the risk of CSFL occurrence up to 2.8 times compared to the initial surgery.

Effect of hydrogel

Other groups investigated the use of absorbable hydrogels for dura repair in spinal procedures with favorable results.[3,30] In this context, cases with complications such as spinal cord compression due to volume expansion or migration of the hydrogel were reported.[19,21,31] In our series, absorbable hydrogels were only used in twelve patients and was always used in combination with other substitutes. Six of these patients developed a CSFL upon

postoperative imaging, but none required treatment for their CSFL, and no adverse affects were observed with regard to the sealant.

Patient characteristics

Analyzing the anatomic location of the lesion and the gender contribution with regard to the incidence of CSFL did not reveal a significant effect in our patient series. However, after the occurrence of CSFL, patients with surgery that involved the cervical spine (23.3%) were at a higher risk of requiring an intervention than CSFL cases that involved the thoracic (7.1%) or lumbar (9.1%) spine. Hannallah et al. showed that cervical spinal patients undergoing revision surgery or presenting with ossification of the posterior longitudinal ligament were more likely to develop incidental CSFL.[15] In the same study, male patients were also at a higher risk of developing CSFL, but age was not a significant factor. In the present study, there was no gender preference regarding the incidence of CSFL, but male patients had a nearly two-fold higher risk of requiring an intervention than female patients (17.4% vs. 8.9%). In contrast, Sin et al. described age as a significant factor of incidental dural tearing in patients undergoing lumbar spinal surgery.[27] Those authors estimate that this might represent the severity of the degenerative changes, which occur throughout the aging process.

Surgical considerations and lesion pathology

In our series, neither the extent of dural opening (Tab. 2, p=0.7) nor the modality by which the dura was opened (Tab. 2, p=0.7) was identified as a significant factor that was correlated with a higher incidence of CSFL. In eleven cases, a dura substitute had to be used to cover larger defects. In these cases, which included 5 meningiomas as the main pathology, the incidence of CSFL was not significantly higher than in the other 79 cases, in which primary suturing of the dura was possible. We did not find any difference in the occurrence of

CSFL in the resected meningiomas, where resection or at least extensive coagulation of the dura is required, as compared to other tumors such as neurinomas or neuroepithelial tumors.

Length of hospital stay (LOS)

The negative medico-economic implications of postoperative CSFL were analyzed by Grotenhuis et al. based on the length of hospital stay after 412 (mainly cranial) interventions.[14] In our study, we did not find a significant difference in terms of the length of hospital stay when the patients were grouped according to outcome. This might be explained in part by the different treatment concepts, with spinal CSF leaks not being treated as aggressively as cranial CSF leaks.

Conclusion

In the present study, none of the applied products appeared to be superior for dura repair when compared to the others. However, surgery with combined use of multiple dura closure substitutes is associated with the enhanced incidence of postoperative CSF leaks, probably due to the more complicated surgical conditions in these cases. Due to the great variety of combinations used and analyzed in this retrospective report, a definite conclusion is not feasible, and a prospective study is required to confirm these results.

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Figure Legend

Figure 1: Number of products used in individual surgical cases. In 7 cases, no product was used, and no CSFL occurred. In most cases (79.1%), at least two products were applied. When 3 or more products were applied, the total number of cases with CSFL exceeded the number of cases without CSFL (p=0.03).

Reviewer 1

Comments to the Author

The authors made important efforts to improve their manuscript, and nearly all of the suggestions are now incorporated in the text.

We still have some objection against the term "optimal" closure, because it potentially claims a level of significance, which can per se not be reached with such a retrospective study design. In fact, the study was done to detect some material being superior to the others, but "optimal" is too strong in the light of this study and it causes expectations, which cannot be fulfilled. My suggestions would be "better" or "superior" instead.

Response

Thank you very much for your response. We agree with the reviewer and changed the term “optimal” to “superior” in the abstract and hope to satisfy the reviewer with the change. We changed the sentence in the abstract to: **“Because many different closure techniques and dura substitutes exist, we analyzed the superior closure to avoid cerebrospinal fluid leaks (CSFL).”**

Reviewer 2

Comments to the Author

Dear authors, please point out more clearly, that your findings concerning the various used dura sealants could not be used to compare those different materials, due to the known bias of the study design and especially the retrospective analysis of your data.

Response

We also agree with this comment from reviewer 2 and changed the manuscript correspondingly. We added the following sentence to the Abstract and Discussion section of the manuscript: **“However, our findings concerning the various dura sealants could not be used to compare those different materials, due to the great variety of combinations of dura sealants and the retrospective analysis of the data.”**